Nephrolithiasis

What the Internist Needs to Know.

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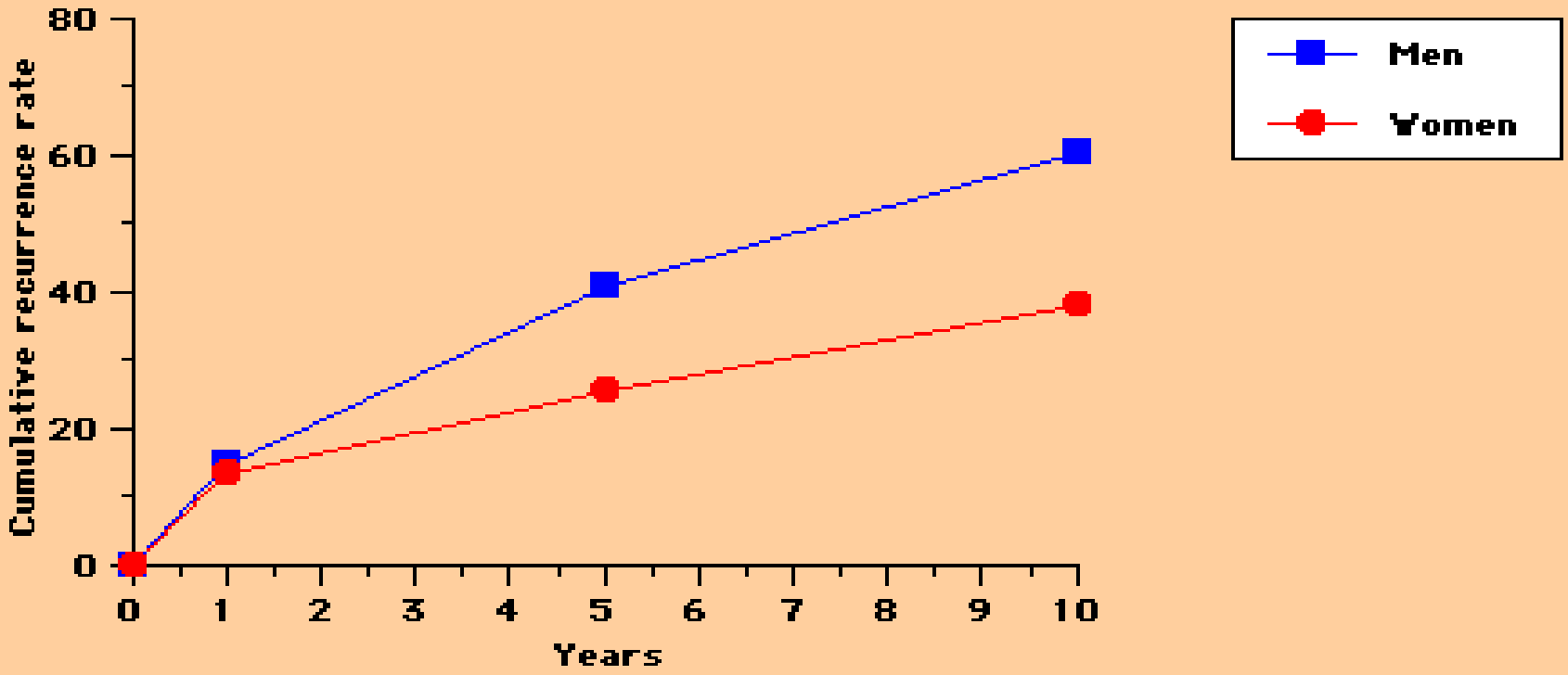
18 Feb 1997

Epidemiology

- Up to 10% in industrialized nations (up to 20% in males)
- Onset typically in 3rd or 4th decade; peak in 5th decade
- Male : Female 3-4 : 1
- Whites >> Blacks
- Approx 10% need hospitalization; 5% surgery

Clinical / Background

- renal colic begins suddenly
- severe flank pain-- radiating to groin
- frequently with nausea, vomiting, gross hematuria and dysuria
- stones < 5mm generally pass spontaneously
- stones > 7 mm usually require surgical intervention



Recurrence rate after first kidney stone Cumulative incidence of stone recurrence after a first kidney stone in men and women. The data represent a summary of six studies. (Data from Uribarri, J, Oh, MS, Carroll, HJ, Ann Intern Med 1989; 111:1006.)

Courtesy of: UpToDate, Rose, BD (ED), UpToDate, Wellesley, MA 1998

Etiology / Incidence / Morphology

I. Calcium Stones-- 70% of all stones

- 26% calcium oxalate
- 37% combination calcium oxalate with calcium phosphate
- 5-10% uric acid core
- 7% pure calcium phosphate
- all are radiopaque

Calcium oxalate crystals Urine sediment showing both dumbbell-shaped calcium oxalate monohydrate (long arrow) and envelope-shaped calcium oxalate dihydrate (short arrows) crystals. Although not shown, the monohydrate crystals may also have a needle-shaped appearance. The formation of calcium oxalate crystals is independent of the urine pH. Courtesy of Frances Andrus, BA, Victoria Hospital, London, Ontario.

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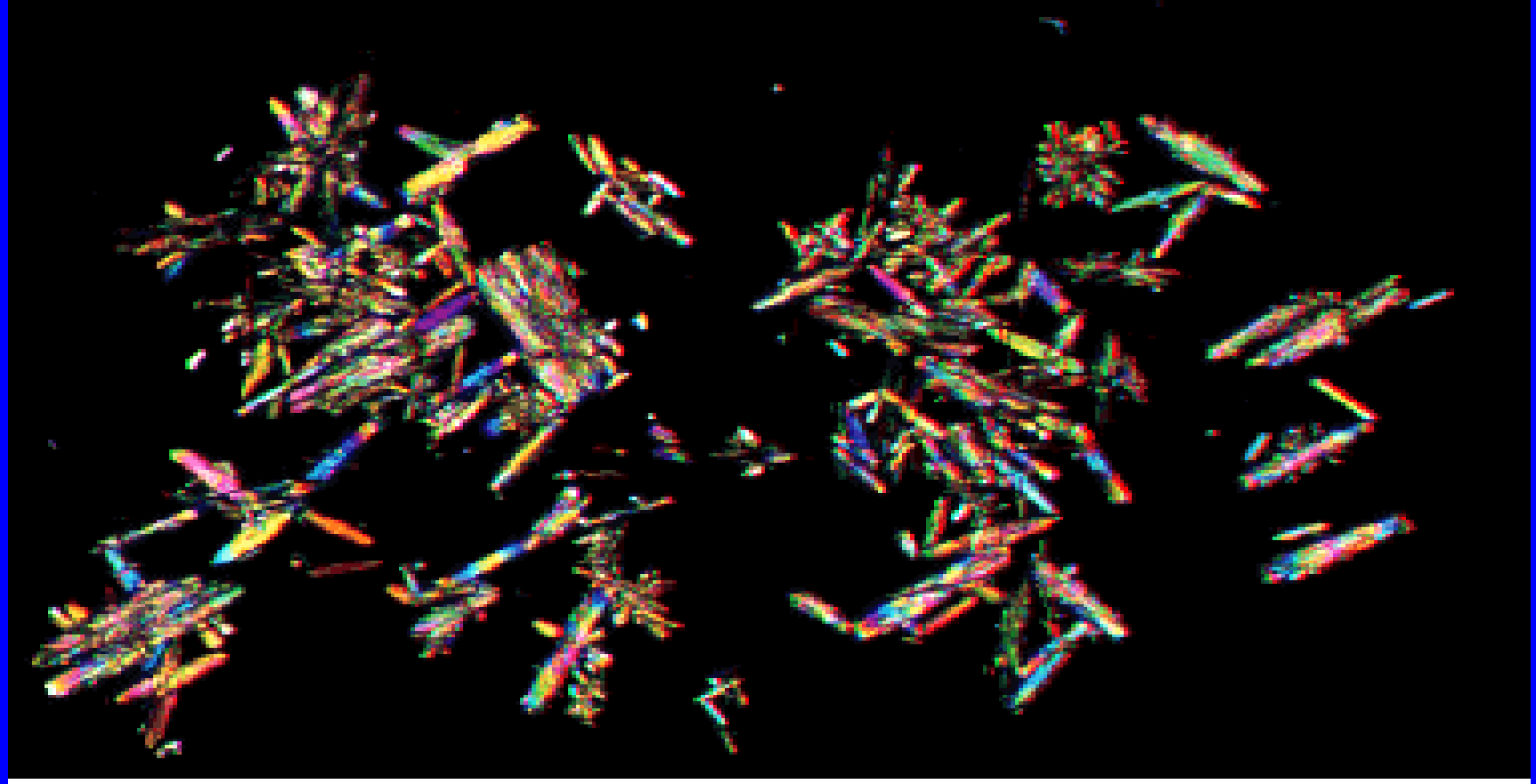


Calcium oxalate monohydrate crystals Urine sediment viewed under polarized light showing coarse, needle-shaped calcium oxalate monohydrate crystals. These crystals have a similar appearance to hippurate crystals. Courtesy of W Merrill Hicks, MD.

Courtesy of: UpToDate, Rose, BD (ED), UpToDate, Wellesley, MA 1998

Main Contributors to Calcium Stones

A. Hypercalciuria

-idiopathic hypercalciuria: most common cause of excessive Ca excretion; responsible for 1/3 of all Ca containing stones

-any disorder that induces even mild hypercalcemia

Etiology of Hypercalcemia

Hypercalcemic disorders:

Primary hyperparathyroidism
Malignancy
Granulomatous diseases
Sarcoid
Thyrotoxicosis
Immobilization

Contributors to Calcium Stones… cont.

B. Hyperoxaluria

-accounts for approx 5% of Ca stones

-nl oxalate excretion = 40mg/day

-urinary oxalate levels > 80mg/day -------

1. Enteric oxaluria- malabsorptive small bowel disease

2. Primary hyperoxaluria- enzyme deficiency

Contributors….cont.

C. Hyperuricosuria

-urate crystals can form a nidus for calcium oxalate crystals

-pt may have excess uric acid excretion (differentiate from pt with uric acid stones who have high uric acid excretion and a low urine pH)

Contributors….cont.

D. Hypocitraturia

-citrate forms highly soluble complex with calcium-- decreases free urine calcium levels

-decreased citrate excretion-- distal RTA, diarrheal d/o’s, diuretic induced hypokalemia, idiopathic

Contributors….cont.

E. RTA

-associated with 3-4% of calcium stones

-distal RTA: non-AG metabolic acidosis with high urine pH, hypokalemia--- enhanced citrate absorption, hypercalciuria, and hyperphosphaturia

Contributors….cont.

F. Anatomic abnormalities of the GU tract

-decreased urine flow / stasis-- can increase of stone formation

Etiology / Incidence / Morphology….cont.

II. Uric Acid Stones

5-10% of all stones (radiolucent)

-uric acid can be increased in pt with high dietary intake and with certain d/o's: gout, myeloproliferative, tumor lysis, Rx's

-suspect in pt with h/o of hyperuricemia and stones seen on IVP or U/S and not KUB

-more important than uric acid level is low urine vol and low urine pH

Urine sediment loaded with uric acid crystals. These crystals are pleomorphic, most often appearing as rhombic plates or rosettes. They are yellow or reddish-brown and form only in an acid urine. Courtesy of Harvard Medical School.

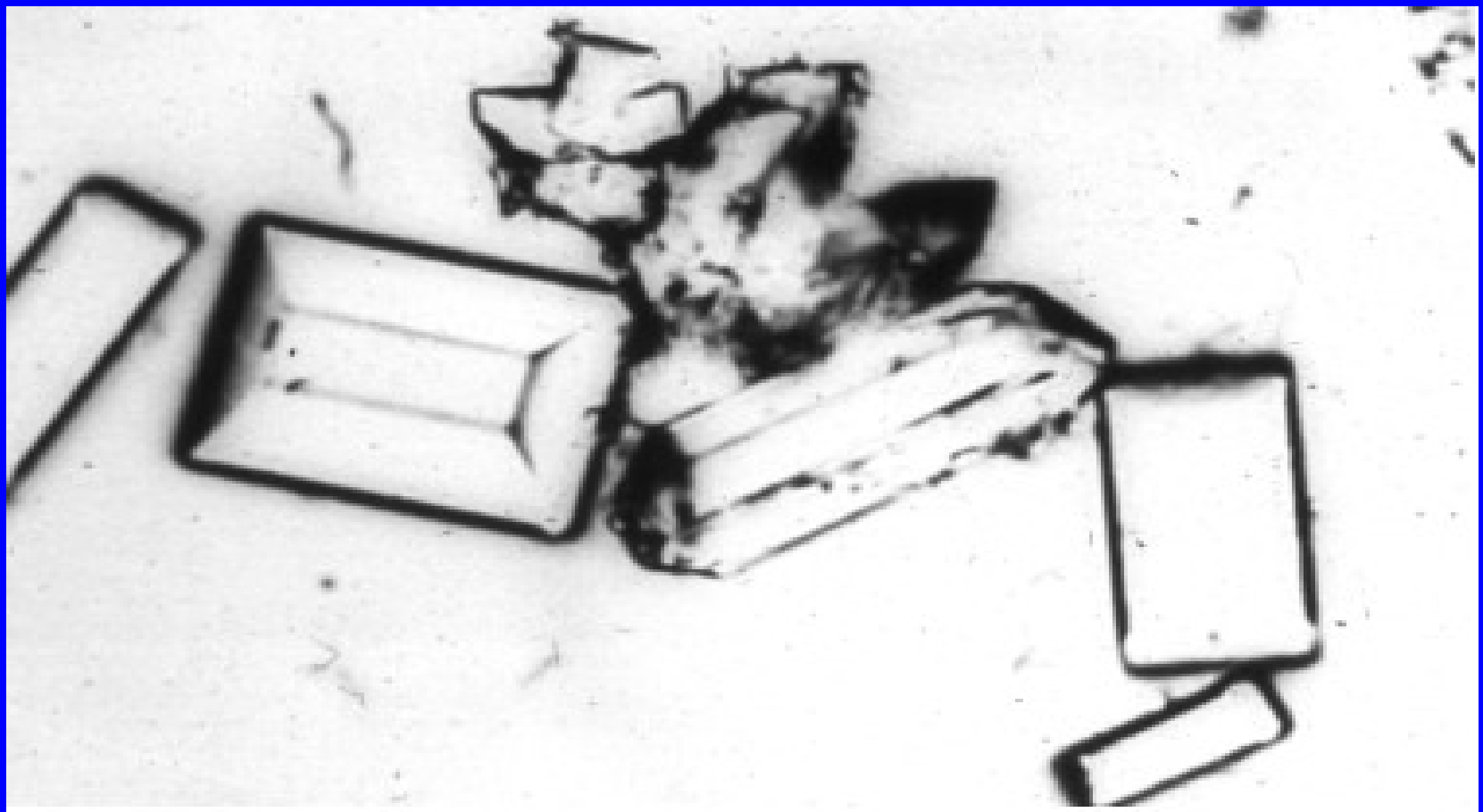
Courtesy of: UpToDate, Rose, BD (ED), UpToDate, Wellesley, MA 1998

Etiology / Incidence / Morphology….cont.

III. Magnesium Ammonium Phosphate Stones (Struvite)

10-15% of all stones; most common cause of staghorn caliculi

-stones develop when increased ammonium concentration coincides with alkaline urine and urinary trivalent phosphate (conditions can only be met when bacterial urease present)



Urine sediment showing multiple "coffin lid" magnesium ammonium phosphate crystals which form only in an alkaline urine (pH usually above 7.0). Courtesy of Harvard Medical School.

Courtesy of: UpToDate, Rose, BD (ED), UpToDate, Wellesley, MA 1998

Plain film of the abdomen (no contrast) showing bilateral radiopaque branched, staghorn calculi filling the collecting systems (arrows). (From Rose, BD, Pathophysiology of Renal Disease, 1st ed, McGraw-Hill, New York, 1981.)

Courtesy of: UpToDate, Rose, BD (ED), UpToDate, Wellesley, MA 1998

Etiology/ Incidence / Morphology….cont.

IV. Cystine Stones

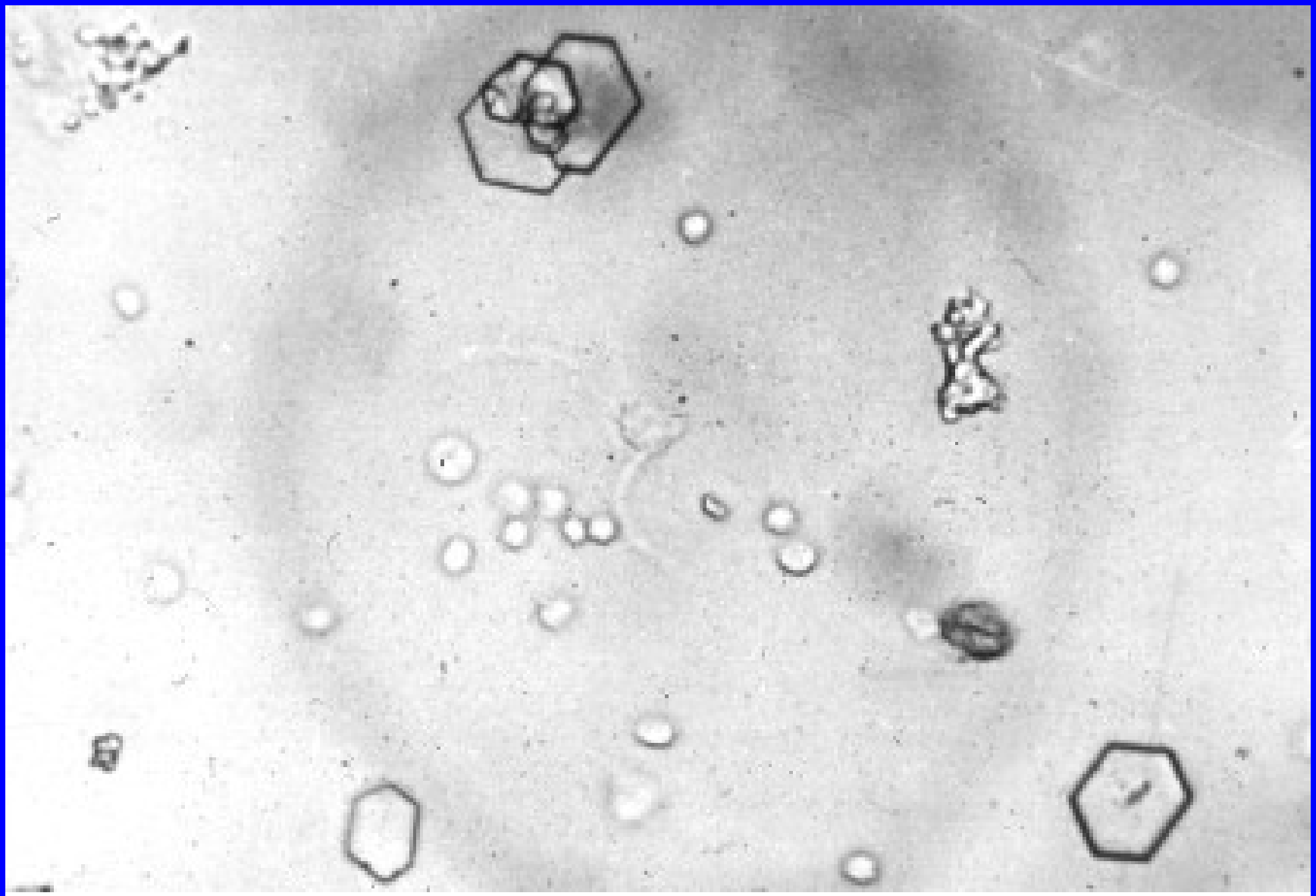
1-2% of all stones

-cystinuria: autosomal recessive trait that generates excessive excretion of cystine

(solubility of cystine 250mg/liter)

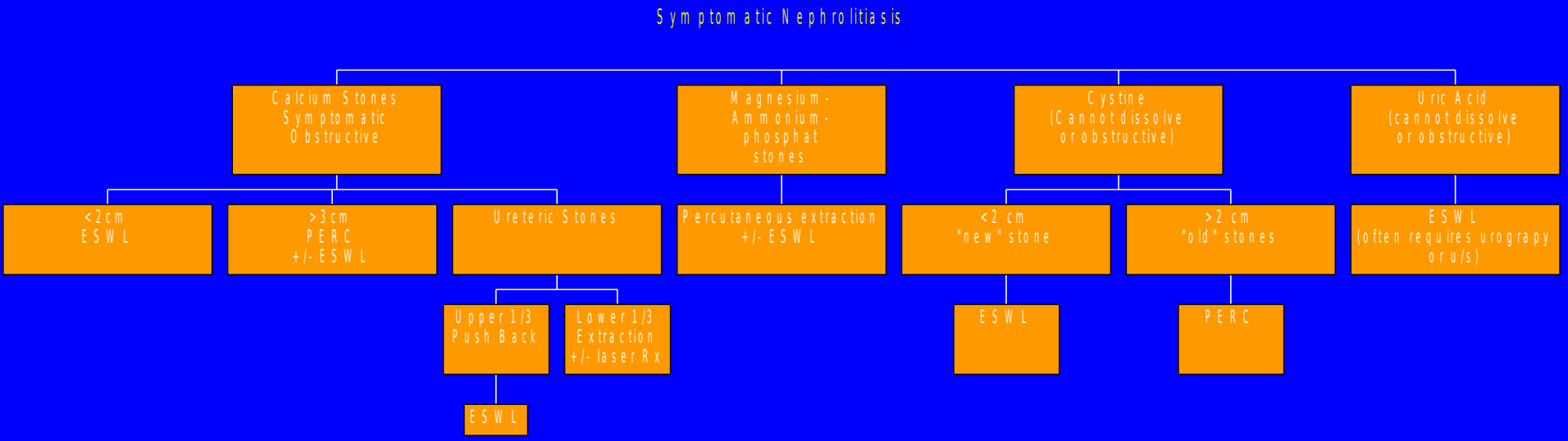
Heterozygote 400-600 mg/day

Homozygote > 600mg/day



Urine sediment showing hexagonal cystine crystals that are essentially pathognomonic of cystinuria. Courtesy of Harvard Medical School.

Surgical Tx Choices



ESWL- extracorpo
real shock wave

Evaluation of Stone Formers

- All patients should have basic eval
- Patients with growing or recurrent stones, in demographic groups in which stones unexpected (non-whites), and all children -- consider comprehensive eval

Basic Evaluation

- History
  - age of first stone
  - number and size of stones
  - frequency of renal colic
  - particular kidney involved
  - spontaneous passage or surgery
  - symptoms

Basic Evaluation….cont.

- PMH (detailed)
- Meds (include OTC’s)
- FMH
- Social History
- Fluid Intake / Dietary History
- Physical Exam

Sulfonamide crystals Urine sediment showing sulfonamide crystals with a needle-shaped appearance. Other forms that may be seen include rosettes and a shock of wheat appearance. Courtesy of Harvard Medical School.

Courtesy of: UpToDate, Rose, BD (ED), UpToDate, Wellesley, MA 1998

Basic Evaluation….cont.

- LABS

  -u/a

  -urine ctx

  -cystine screening

  -Ca, Phos, Uric Acid, P1, PTH (if indicated)
- Radiology

  -KUB / IVP / Ultra Sound / CT

The Complete Evaluation = Basic Evaluation + 24hr Urine Studies

- Pt with “metabolically active” stones
- Urine Studies, 24hr collection for:

  Volume, Ca, Oxalate, Na, Phos, Uric Acid, Citrate, and Creatinine (add cystine if screening + or no screening available)

24 hour urine should be deferred for 6 weeks after stone passage

- Repeat x 2 if values normal; if remains normal x 3 collections--- “ Idiopathic Nephrolithiasis”

Non-Specific Therapy

- increase po intake to double u.o. or > 2 liters/day
- decrease protein intake to 0.8 - 1.0 gm / day
- decrease Na to 2 - 3 gm / day
- limit Ca intake (approx 1gm / day)-- only in pt with hypercalciuria with excess intake or those remaining hypercalciuric despite tx.

Specific Therapy

A. Calcium Stones

1st visit: complete eval vs basic eval

2nd visit: review data and tx accordingly

-initiate non-specific tx if no specific disorder identified; repeat 24 hr urine if complete eval initiated and original studies negative.

3rd visit: review data and results of non-specific tx; continue vs specific tx

Tx: Calcium Stones….cont.

- assess Na restriction with 24 hr urine
- repeat KUB if not done in 2 months
- further tx based on stone composition and abnormalities noted on 24hr urine……..

Hypercalciuria….tx.

- Thiazide diuretics
- Cont to stress Na restriction
- Supplement K if needed

- Once hypercalciuria controlled, f/u q 6-12 months with 24hr urine and KUB
- If hypercalciuria can not be managed with above, consider Ca restricted diet (800-1000mg)

Hyperoxaluria….tx.

TX depends on cause

-mild dietary hyperoxaluria: tx with diet restriction

-enteric hyperoxaluria:

increase volume intake

tx underlying cause of malabsorption

restrict dietary oxalate

calcium supplement with meals

Hyperoxaluria tx….cont.

Diarrhea-- may lead to hypokalemia, hypomagnesemia, and met acidosis-- hypocitraturia

tx: potassium citrate (20-30meq tid) and Mg gluconate (0.5-1.0gm tid)

Primary Hyperoxaluria: tx with increased vol intake, and with pyridine, citrate, Mg, and orthophosphate supplementation

Hypocitraturia….tx.

Tx: potassium citrate; 15-25meq po bid-tid, often require > 320meq / day

RTA….tx.

Tx: potassium citrate or potassium bicarbonate (120 meq/day in 2 - 3 divided doses often required)

Hyperuricosuria….tx.

Hyperuricosuric calcium oxalate stones- tend to have excessive urinary urate, nl uric calcium and oxalate concentration, and urine pH > 5.5

Tx: increase fluid intake, low purine diet; if uricosuria remains poorly controlled, can tx with allopurinol (100-300mg po qd)

Specific Therapy….cont.

B. Uric Acid Stones

1st visit: complete eval

2nd visit: review data; nonspecific therapy-- u.o. > 3liters/d; low purine and animal prot diet

-potassium citrate 30 meq bid to increase urine pH to approx 6.5 (excess alkalization can lead to Ca/PO4 stones)

Specific Tx: Uric Acid Stones….cont.

Subsequent Visits:

-repeat 24 hr urine studies; check urine pH

-reinforce vol intake

-if urine pH < 6.0 on large doses of potassium citrate, check compliance with rx and diet

-consider allopurinol if urine pH remains low or uric acid excretion cont to be >1000mg / day; start at 100mg q day

Specific Therapy….cont.

C. Sturvite Stones

-diagnosis made by several associated findings: Urine pH > 7.0; positive urine ctx for urease producing bacteria; staghorn caliculi, and/or h/o struvite stones

Refer to Urologist as soon as diagnosis made.

Specific Tx: Struvite Stone….cont.

Once stone free:

-culture specific atbx at therapeutic doses until urine sterile, then cont at 1/2 therapeutic dose until culture negative for 3 consecutive months, then d/c atbx.

-monthly surveillance ctx's for one year

-consider low phosphate diet and phosphate binder with meals

Specific Therapy….cont.

D. Cystine Stones

-tx aimed at increasing solubility of cystine in urine

-hydration main therapy

-if pt has < 500mg cystine excretion/day; then > 2 liter/day may effectively decrease precipitation

-Low Na/prot diet can also decrease cystinuria

Specific Tx: Cystine Stones….cont.

-if pt has > 500 mg cystine/day or who excretes > 250mg/day on nonspecific therapy, then consider d-Penicillamine (chelating agent)

-Thiola (alpha-Mercaptopropionylycine) and Rinatil (Bucillamine)-- new chelators with less side effects

-cystine stones require surgical removal